

REMARKS

Claim status

Claims 1 and 11 are amended herein, without prejudice or disclaimer of Applicants right to pursue any canceled subject matter in a continuing application.

Claim rejections

35 U.S.C. § 112

Claims 1-11, 13-14, 19-21, 24-30, and 32 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. In particular, the Office Action states it is unclear what amount is deemed “generally” equivalent. Without acquiescing to the allegation, and solely for the purposes of expediting prosecution, claims 1 and 11 have been amended to delete recitation of “generally.” Accordingly, the rejection on this basis is rendered moot and Applicants respectfully request withdrawal of the same.

35 U.S.C. §§ 102, 103

Claims 1, 2, 3, 7-12, 24, 25, and 27-30 were rejected under 35 U.S.C. § 102 as allegedly anticipated by U.S. Patent No. 5,731,171 (hereinafter “Bohlander”). Claims 1-3, 5, and 7-10 are rejected under 35 U.S.C. §102 as allegedly anticipated by U.S. Patent Publication No. 2003/0073081 (hereinafter “Mukai”). Further, claims 13, 14, 19-23, and 26 are rejected under 35 U.S.C. §103 as allegedly obvious over Mukai in view of U.S. Patent No. 6,783,940 (hereinafter “McLaughlin”). In particular, it is stated that Bohlander discloses a reagent composition comprising “each of dATP, dCTP, dGTP, and dTTP . . . in combination with . . . 40 µM Bio-11-dUTP,” and that Mukai discloses ““0.625 mM each of dATP, dCTP, and dGTP, 0.625 mM of a dTTP+Aminoallyl dUTP mixture,”” and thus that each reference individually anticipates the reaction mixture of claim 1. *OA*, at pp. 5-7 (emphasis added).

In response to Applicants submission that the present claims are directed toward deoxyuridine triphosphate (dUTP), whereas both Bohlander and Mukai disclose the use of a conjugated dUTP, e.g., Bio-11-dUTP or Aminoallyl-dUTP, it is alleged that “the generic recitation of dUTPs cover all species therein, including but not limited to conjugated dUTPs.” *OA*, at pp. 5, 8. However, such allegation erroneously (1) assumes that the plain and customary definition of dUTP encompasses functionalized/conjugated dUTP, (2) disregards the definition

of dUTP as set forth by the Applicant, (3) interprets dUTP more broadly than is reasonable in light of the specification, and (4) ignores a wherein clause indicating that the inclusion of dUTP reduces the formation of primer aggregates during the amplification reaction in comparison with an amplification reaction employing only conventional nucleotides.

For the record, Applicants respectfully assert that the Office has mistakenly construed the ordinary and customary meaning of dUTP to encompass a functionalized/conjugated dUTP. The term “dUTP” is merely a well-known abbreviation for the nucleic acid deoxyuridine triphosphate and, absent any teaching to the contrary, cannot automatically be interpreted to include functionalized/conjugated dUTP absent adequate basis in the specification. If the ordinary and customary meaning of dUTP were to encompass a functionalized/conjugated dUTP, the ordinarily skilled artisan would not have to distinguish between unfunctionalized/unconjugated dUTP and functionalized/conjugated dUTP. Furthermore, a patent drafter would not have to change the definition of dUTP to include functionalized/conjugated dUTP.

However, since an ordinarily skilled artisan would not understand dUTP to encompass functionalized/conjugated dUTP, the art consistently uses different notations for unfunctionalized/unconjugated dUTP and functionalized/conjugated dUTP (e.g., Bio-11-dUTP, Aminoallyl-dUTP, etc.). Indeed, each of the cited references refers to the functionalized/conjugated dUTP by the conjugated functional group. *See, Bohlander*, at Col. 16 lines 17-26 (stating the amplified product was biotin-labeled with Bio-11-dUTP) (emphasis added); *see also id. col. 20, lines 46-67* (referring to Bio-11-dUTP and Spectrum-Orange - dUTP); *see also, Mukai*, at paragraph [0326] (distinguishing between dUTP and a derivative having a functional group such as dUTP having an amino acid group); *see also id.* at paragraph [0954]-[0961] (consistently referring to aminoallyl dUTP to bring an amino group into the amplification product).

Furthermore, since an ordinarily skilled artisan would not understand dUTP to encompass functionalized/conjugated dUTP, patent disclosures often explicitly, deliberately, and precisely set forth an uncommon definition of “dUTP” as encompassing both deoxyuridine triphosphate and functionalized/conjugated dUTP. *See, e.g.*, M.P.E.P. § 2111.01 (citing *In re Paulsen*, 30 F.3d 1475, 1480, 31 USPQ2d 1671, 1674 (Fed. Cir. 1994) (inventor may define specific terms used to describe invention, but must do so "with reasonable clarity, deliberateness, and precision" and, if done, must "set out his uncommon definition in some manner within the patent

disclosure' so as to give one of ordinary skill in the art notice of the change" in meaning) (quoting *Intellicall, Inc. v. Phonometrics, Inc.*, 952 F.2d 1384, 1387-88, 21 USPQ2d 1383, 1386 (Fed. Cir. 1992)). Indeed, McLaughlin explicitly, deliberately, and precisely sets forth an uncommon definition of the term "dNTPs" by stating that conjugated dNTPs are encompassed by the term. *See, e.g., McLaughlin*, at Col. 6, lines 20-15. In light of the above, Applicants respectfully request that the term dUTP be ordinarily and customarily construed to encompass deoxyuridine triphosphate, and not functionalized/conjugated dUTP.

Regardless of whether the Office agrees that the ordinary and customary meaning of dUTP excludes functionalized/conjugated dUTP, Applicants also assert that an interpretation otherwise erroneously disregards the definition of dUTP as set forth by the Applicants. *See, e.g., M.P.E.P. § 2111.01* (stating Applicant is entitled to be his or her own lexicographer and may set forth a definition of a term). As taught by the M.P.E.P., the specification should be relied on for more than just explicit lexicography or clear disavowal of claim scope to determine the meaning of a claim term when applicant acts as his or her own lexicographer; the meaning of a particular claim term may be defined by implication, that is, according to the usage of the term in the context in the specification. *See, id.* (citing *Phillips v. AWH Corp.*, 415 F.3d 1303, 75 USPQ2d 1321 (Fed. Cir. 2005) (en banc); and *Vitronics Corp. v. Conceptronic Inc.*, 90 F.3d 1576, 1583, 39 USPQ2d 1573, 1577 (Fed. Cir. 1996)). Here, Applicants have consistently asserted that dUTP refers only to deoxyuridine triphosphate. Also, the specification consistently uses dUTP to refer only to deoxyuridine triphosphate. In fact, the specification specifically indicates that dUTP is an abbreviation for deoxyuridine triphosphate. *Id.* at paragraph [0011]. Furthermore, the specification completely lacks any teaching or suggestion that dUTP may refer to a functionalized/conjugated dUTP. Indeed, in stark contrast to the cited art (particularly Mukai and McLaughlin) the specification did not set forth any definition for dUTP that would clearly, deliberately, and precisely include functionalized/conjugated dUTP.

Applicants further note that a claim term must be given its broadest reasonable interpretation in light of the specification. *See, e.g., M.P.E.P. § 2111.01* (citing *In re American Academy of Science Tech Center*, 367 F.3d 1359, 1369, 70 USPQ2d 1827, 1834 (Fed. Cir. 2004); *In re Zletz*, 893 F.2d 319, 321, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989); *Chef America, Inc. v. Lamb-Weston, Inc.*, 358 F.3d 1371, 1372, 69 USPQ2d 1857 (Fed. Cir. 2004)) (emphasis added). Here, the specification teaches that dUTP was used in the prior art in combination with an

enzymatic degradation step employing UNG or other like enzyme to degrade uracil-containing amplicons. *See, e.g., id.*, at paragraphs [0008]-[0010], [0067]. Applicants respectfully assert that the prior art use of dUTP did not include use of functionalized/conjugated dUTP in combination with a uracil DNA glycosylase to degrade uracil-containing amplicons. Indeed, even Mukai distinguishes between use of dUTP for enzymatic degradation of amplicons and use of functionalized dUTP for the incorporation of the functional group. *See, Mukai*, at paragraph [0404] (stating “if dUTP is used as a substrate, it is possible to prevent carry-over contamination of amplification products by degrading amplification products using uracil N-glycosidase (UNG)) and at paragraph [0954] (stating “an ICAN reaction was carried out using Aminoallyl dUTP . . . in order to introduce an amino group into the ICAN amplification product.”). Accordingly, the term dUTP as used in light of the specification disclosure related to the prior art does not reasonably include functionalized/conjugated dUTP.

Further, the specification teaches that unlike the prior art, the present invention uses dUTP to reduce formation of primer aggregates. Applicants also respectfully assert that a skilled artisan reading the specification would not interpret dUTP to include functionalized/conjugated dUTP since a functionalized/conjugated dUTP is unlikely to reduce the formation of primer aggregates. Accordingly, Applicants respectfully assert that even the broadest reasonable interpretation of “dUTP” in light of the specification disclosure related to the present claims would not include a functionalized/conjugated dUTP.

Applicants also respectfully assert that the wherein clause of claims 1 and 11 must be given patentable weight. In contrast to the prior art disclosures, the present invention employs dUTP to reduce the formation of primer aggregates. Such distinction is captured by the respective recitations of “wherein the inclusion of dUTP reduces the formation of primer aggregates during the amplification reaction in comparison with an amplification reaction employing only conventional nucleotides” and “wherein the level of primer aggregate formed during the amplification step is reduced as compared to amplifying the target nucleic acid using a dNTP mix having only conventional nucleotides” in claims 1 and 11. Since the wherein clause in both claim 1 and claim 11 relates back to and clarifies what is required by the claim, it should be given a limiting effect. *See, e.g.*, M.P.E.P. § 2111.04 (stating “when a ‘whereby’ clause states a condition that is material to patentability, it cannot be ignored in order to change the substance of the invention”); *see also Griffin v. Bertina* 285 F.3d 1029, 1033-34 (holding that the wherein

clause at issue must be given limiting effect because it relates back to and clarifies what is required by the claim.)) In other words, the claims should be read as requiring that the dUTP in the composition reduce the formation of primer aggregates.

As detailed above, the recitation dUTP in the present claims does not encompass functionalized/conjugated dUTP, and an interpretation otherwise is contrary to established case law for at least four reasons. Since Bohlander and Mukai only teach functionalized/conjugated dUTP for the introduction of a functional group and Mukai teaches dUTP in the presence of a uracil degradation enzyme, neither reference anticipates the present claims.

It is alleged that lack of a “uracil degradation enzyme” does not overcome the rejections over Mukai because “the mixture at [sic] point prior to addition of UDG or UNG would still anticipate the mixture of the claimed invention.” *OA*, at pp. 6, 9. Applicants respectfully direct attention to the specification as filed at paragraph [0067], “UNG treatment was performed on PCR reactions before dUTP was added to ensure that any contaminant UTP containing product was degraded before the next reaction, thereby enhancing the reaction specificity.” Applicants note that there is no teaching to the contrary in any of the cited references. Accordingly, a composition comprising dUTP would necessarily comprise UDG or UNG. In other words, there is no point prior to the addition of UDG or UNG in which the compositions taught by the cited references would anticipate the present claims.

Having distinguished the independent claims from the art of record, Applicants respectfully submit that the claims dependent there from are patentable for at least the same reasons. However, Applicants reserve the right to separately address the patentability of the dependent claims in the future, should that be necessary. Reconsideration and withdrawal of the rejections is respectfully requested.

CONCLUSION

Applicants respectfully submit that the instant application is in condition for allowance. Entry of the amendments and an action passing this case to issue is therefore respectfully requested. Should there be any remaining issues that remain unresolved, the Examiner is encouraged to telephone the undersigned at (415) 356-3064.

Respectfully submitted,
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